IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 8727
KIM *et al.*	Art Unit: 1627
Appl. No.: 10/646,145	Examiner: SOROUSH, Layla
Filed: August 22, 2003	Atty. Docket: 2298.0140001/TJS/M-N
For: **Composition Comprising the Extract of Actinidia Arguta and Related Species for the Prevention and Treatment of Allergic Disease and Non-Allergic Inflammatory Disease**	

Declaration of Sunyoung Kim Under 37 C.F.R. § 1.132

Mail Stop Amendment

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

The undersigned, Sunyoung Kim, Ph.D., residing at 390 Egok-ri Soheul-eup Pocheon-si, GyeongGi-Do, Korea 487-821, declares and states as follows:

1. I am a professor of the Seoul National University. I am also a major inventor listed in the above-captioned patent application. My credentials are provided in the *curriculum vitae* that is attached to this declaration as Exhibit A. I received my Ph.D. degree in Molecular Genetics, from the University of Oxford. As seen from my attached *curriculum vitae*, I have extensively investigated the therapeutic uses of various natural products, and have particular expertise in isolating fruit extracts for the treatment of inflammatory diseases. I have published several papers related to the development of fruit extracts for disease treatment.

2. It is my understanding that the kiwifruit extract discussed in U.S. Patent No. 6,630,163 ("Murad"), which was cited against U.S. Appl. No. 11/522,511, is an extract of *Actinidia deliciosa.*

3. The results presented in Exhibit B, described below, provide a side-by-side comparison of the effects of the extract of *Actinidia arguta*, *i.e.*, the kiwifruit extract recited in the currently pending claims, and the extract of *Actinidia deliciosa, i.e.*, the kiwifruit extract discussed in Murad, on IgE production in U266B1 cells and IL-4 and IL-5 production in ovalbumin (OVA)-sensitized splenocytes from BALB/c female mice. The data presented herewith was obtained by Viromed Co., Ltd.

4. The following is a description of studies comparing the effects of *Actinidia arguta* and *Actinidia deliciosa* extracts. *Actinidia arguta* and *Actinidia deliciosa* fruits were purchased from a farm specializing in the cultivation of *Actinidia arguta* (Hurstberry, Oregon, USA) and a supermarket, respectively. After air-drying, it was determined that the fruits had a moisture content of <10%. The dried fruit (10g) was extracted three times by heat treatment in distilled water (DW) to yield a water-soluble extract. The water-soluble extract was filtered (No. 2 Filter Paper; 110 mm, Whatman), concentrated using a rotary evaporator, and freeze-dried. Freeze-dried extracts were then dissolved in DW at a concentration of 100 mg/mL and stored at –80 °C until they were ready for use.

5. U266B1 cells (human B cell line useful for studying allergic responses *in vitro*) were cultured in 24 well plates (2×10^5 cells/well) in RPMI-1640 medium supplemented with 10 % FBS, 2 mM L-glutamine, 10 mM HEPES, 1 mM sodium pyruvate, 50 μg streptomycin, and 100 U/ml penicillin (all from Life Technologies) at 37 °C under 5% CO_2. Cells were treated with an allergen, lipopolysaccharide ("LPS") (2 μg /ml), and *Actinidia arguta* or *Actinidia deliciosa* extracts (500 μg/ml). After 7 days of

culture, the cell supernatants were collected to measure the level of IgE in the supernatants by ELISA (total human IgE; AlerChek). The results were expressed as a percentage of inhibitory activity on LPS-mediated IgE production.

6. As shown in Exhibit B, the extract of *Actinidia arguta* decreased the LPS-mediated production of IgE by 70%, while the extract from *Actinidia deliciosa* inhibited IgE production by only 37%. The difference between the levels of IgE inhibition by extracts of *Actinidia arguta* and *Actinidia deliciosa* is statistically significant at $p<0.05$. These results demonstrate that the *Actinidia arguta* extract is approximately 2-fold more potent than the *Actinidia deliciosa* extract at inhibiting IgE production. Accordingly, these results clearly demonstrate the superior ability of the *Actinidia arguta* extract to reduce IgE production as compared to the *Actinidia deliciosa* extract discussed in Murad.

7. BALB/c female mice (7 weeks old) were individually immunized and later boosted by intraperitoneal (i.p.) injections of 20 μg of ovalbumin "(OVA") (grade V; Sigma) emulsified in 2.25 mg of aluminum hydroxide (ImjectAlum; Pierce) on day 0 and day 14, respectively. Non-sensitized (naive) mice did not receive any reagent. On day 24, both OVA-sensitized and naive mice were sacrificed (n=5/group), and the spleens of these animals were isolated to study the production of cytokines in splenocytes using the recall response. Briefly, spleens in each group of mice were obtained, pooled and homogenized under sterile conditions. Splenocytes were filtered through a 60 μm pore nylon sieve to remove large aggregates, washed with HEPES-buffered RPMI-1640 medium, and centrifuged at 1500 rpm for 5 min. After centrifugation, the supernatant was discarded, and the splenocytes were resuspended in

culture medium (RPMI-1640 containing 10% heat-inactivated FBS). The resulting splenocyte suspension was seeded into a 24 well culture plate, while adjusting the final concentration of splenocytes to 5×10^6 cells/ml/well. Splenocytes were incubated with 100 μg/ml of OVA in the presence of *Actinidia arguta* or *Actinidia deliciosa* extract (1 mg/ml, respectively), or media as a control for 3 days. Following incubation, the splenocyte culture supernatants were collected to detect the level of IL-4 and IL-5 using respective ELISA kits (Endogen).

8. As shown in Exhibit C, the extract of *Actinidia arguta* significantly decreased the OVA-stimulated production of IL-4 by 70%, while the extract of *Actinidia deliciosa* inhibited IL-4 production by only 29%. The difference between the levels of IL-4 reduction by extracts of *Actinidia arguta* and *Actinidia deliciosa* is statistically significant at $p<0.05$. These results demonstrate that the *Actinidia arguta* extract is about 2.5-fold more potent than the *Actinidia deliciosa* extract at inhibiting IL-4 production. Accordingly, these results clearly demonstrate the superior ability of the *Actinidia arguta* extract to reduce IL-4 (Th2 cytokine) production as compared to the *Actinidia deliciosa* extract.

9. In conclusion, the results presented in Exhibits B and C clearly demonstrate the superior and unexpected abilities of the extract of *Actinidia arguta* to reduce IgE and Th2 cytokine production as compared to the extract of *Actinidia deliciosa*.

10. I further declare that the above statements made of my own knowledge are true and the above statements based on information and belief obtained from the references and documents discussed are believed to be true. Additionally, I declare that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Title 18 United States Code Section 1001, and that willful false statements may jeopardize the validity of this application or any patent issuing thereon.

11. I have read, I am familiar with, and I understand, the provisions of 37 C.F.R.§§ 11.18(b) and (c) relating to the effect of signature and certificate for correspondence filed in the U.S. Patent and Trademark Office.

Date: Aug 18, 2010

Sunyoung Kim, Ph.D.

Exhibit A

CURRICULUM VITAE

Name : Sunyoung Kim
Position: Professor
Institution : School of Biological Sciences, Seoul National University

Academic Degrees:

1978	Microbiology	B.S.	Seoul National University
1982	Biochemical Engineering	M.S.	MIT
1984	Microbiology and Molecular Genetics	M.A.	Harvard University
1986	Molecular Genetics	D. Phil	University of Oxford

Professional Activities (Selected):

1987-1989	Postdoctoral fellow Whitehead Institute for Biomedical Research, and Department of Biology, MIT (with Dr. David Baltimore)
1990-1992	Assistant Professor of Medicine (Virology) Harvard University
1992- Present	Professor Seoul National University
1998-present	Member of the Editorial Board Journal of Gene Medicine (John Wiley & Sons Ltd.)
2003-2008	Member of the Editorial Board Gene Therapy (Nature Publishing Group)
2006-2008	President Korea Society of Gene Therapy
2005-2009	Chief Executive Officer, Founder ViroMed Co. Ltd. (Korea)

Publications:

89. K. Koh, Y. Cha, **S. Kim**, and J. Kim (2009) tBHQ inhibits LPS-induced microglial activation via Nrf2-mediated suppression of p38 phosphorylation. *Biochem Biophys Res Commun.*,380(3):449-53.

88. Donghyun Kim, Seon Hee Kim, Eun-Jin Park, Chang-Yuil Kang, **Sunyoung Kim** (2009) Suppression of allergic diarrhea in murine OVA-induced food allergy model by PG102, a water-soluble extract prepared from Actinidia arguta. *International Archives of Allergy and Immunology*,150(2):164-71.

87. Kyungmi Koh, Karim Lee, Jinhyun Ahn, **Sunyoung** Kim (2009) Human cytomegalovirus infection downregulates the expression of glial fibrillary acidic protein in human glioblastoma cells, U373MG : Identification of viral genes and protein domains involved. *Journal of General Virology*, 90(Pt 4):954-62.

86. Donghyun Kim, Seon Hee Kim, Eun-Jin Park, Chang-Yuil Kang. **Sunyoung Kim** (2009) Anti-allergic effects of PG102, a water-soluble extract prepared from Actinidia arguta, in a murine OVA-induced asthma model. *Clinical & Experimental Allergy*,39(2):280-9.

85. Youngtae Hong, Seung Shin Yu, Nam-Kyung Yoon, Sung June Kang, Jun-Tae Lee, Sujeoung Kim, Jong-Mook Kim, Karim Lee, Ji-Won Jang, **Sunyoung Kim** (2008.8) Development of an in vitro cell culture assay system for measuring the activation of a neighbouring gene by the retroviral vector. *The Journal of Gene Medicine*,10(8):847-54.

84. **Sunyoung Kim**, Zhaohui Peng and Yasufumi Kaneda (2008.2) Current Status of Gene Therapy in Asia. *Molecular Therapy*,16(2):237-43.

83. H.J. Choi, H. Eo, K.C. Park, M. Jin, E-J Park, S.H. Kim, J.E. Park, and **S. Kim** (2007.8) A water-soluble extract from Cucurbita moschata shows anti-obesity effects by controlling lipid metabolism in a high fat diet-induced obesity mouse model. *Biochem Biophys Res Commun.*,359(3):419-25.

82. E-J Park, K.C. Park, H. Eo, J. Seo, M. Son, K.H. Kim, Y-S Chang, S-H Cho, K-U Min, M. Jin, and **S. Kim** (2007.5) Suppression of spontaneous dermatitis in NC/Nga murine model by PG102 isolated from Actinidia arguta. *Journal of Invetigative Dermatology*,127(5):1154-60.

81. J-T Lee, S. S. Yu, V. N. Kim, and **S. Kim** (2007.1) Control of Splicing Efficiency by the Mouse Histone H2a Element in an MLV-Based Retroviral Vector. *Molecular Therapy*,15(1):167-72.

80. JM Kim, BK Lim, SH Ho, SH Yun, JO Shin, EM Park, DK Kim, **S. Kim**, and ES Jeon (2006.6) TNFR-Fc fusion protein expressed by in vivo electroporation improves survival rates and myocardial injury in coxsackievirus induced murine myocarditis.*Biochem Biophys Res Commun.*, 344: 765-771.

79. S. Kim, K. Lee, M-D Kim, S. Kang, C.W. Joo, J-M Kim, S.H. Kim, S.S. Yu, and **S. Kim** (2006.5) Factors affecting the performance of different long terminal repeats in the retroviral vector. *Biochem Biophys Res Commun.*, 343: 1017-1022.

78. S. Ho, H. Lee, D. Kim, J. Jeong, S. Kim, S.S. Yu, Z. Jin, **S. Kim**, and J.Kim (2006. 5) Intrasplenic electro-transfer of IL-4 enciding plasmid DNA efficiently inhibits rat experimental allergic encephalomyelitis. *Biochem Biophys Res Commun.*, 343: 816-824.

77. J.J. Choi, M. Jin, J.K. Lee, W.Y. Lee, Y-I Park, Y.N. Han and **S. Kim** (2006. 01) Control of cytokine gene expression by PG101, a water-soluble extract prepared from Lentinus lepideus. *Biochem Biophys Res Commun.*, 339: 880-887.

76. E-J Park, B. Kim, H. Eo, K. Park, Y. Kim, H.J. Lee, M. Son, Y-S Chang, S-H Cho, **S. Kim** and M. Jin (2005. 11) Control of IgE and selective Th1 and Th2 cytokines by PG102 isolated from Actinidia arguta. *J. Allergy Clinical Immunol*, 116:1151-1158

75. K. Lee, K. Jeon, J.M.Kim, V.N.Kim, D.H.Choi, S.U.Kim and **S. Kim** (2005. 7)

Downregulation of GFAP, TSP-1 and p53 in human glioblastoma cell line, U373MG, by IE1 protein from human cytomegalovirus: Implications for the possible role of IE1 in the pathogenesis of glioma. *GLIA*, 51:1-12.

74. K.C. Park, E.J. Park, E.R. Kim, Y. Kim, S.H. Chung, B.W. Cho, **S. Kim** and M. Jin (2005. 6) Therapeutic effects of PG201, an ethanol extract from herbs, through cartilage protection on collagenase-induced arthritis in rabbits. *Biochem Biophys Res Commun.*, 331(4):1469-77.

73. J.G. Jeong, J.M. Kim, S.H. Ho, W. Hahn, S.S. Yu, and **S. Kim** (2004.10) Electrotransfer of Human IL-1Ra into Skeletal Muscles Reduces the Incidence of Murine Collagen-induced Arthritis. *J. Gene Medicine*, 6:1125-1133.

72. Y. Hong, K. Lee, S.S. Yu, S. Kim, and **S. Kim** (2004.07) Factors affecting retrovirus-mediated gene transfer to human CD34+ cells. *J. Gene Medicine*, 6:724-733.

71. S.Kim, E.J.Park, S.S.Yu, **S. Kim** (2004.06) Development of enzyme-linked immunosorbent assay for detecting antibodies to replication-competent murine leukemia virus. *J. Virological Methods*, 118:1-7

70. Y.S. Na, K.Yoon, J.G. Nam, B. Choi, J.S. Lee, I. Kato, and **S. Kim** (2004.06) Nef from a primary isolate of human immunodeficiency virus type 1 lacking the EE(155) region shows decreased ability to downregulate CD4. *J. General Virology*, 85: 1451-61

69. W. Hahn, S.H. Ho, J.G. Jeong, E.Y. Hahn, S.S. Yu, **S. Kim**, J.M. **Kim** (2004.05) Viral vector-mediated transduction of a modified thrombospondin-2 cDNA inhibits tumor growth and angiogenesis. *Gene Therapy*, 11: 739-45

68. J. Lee, S. S. Yu, E. Han, S.J. Kim, and **S. Kim** (2004) Engineering the Splice Acceptor for Improved Gene Expression and Viral Titer in an MLV-based Retroviral Vector. *Gene Therapy*, 11: 94-9

67. J-M Kim, J-G Jeong, S-H Ho, W Hahn, E-J Park, S Kim, SS Yu, Y-W Lee, and **S Kim** (2003) Protection against collagen-induced arthritis by intramuscular gene therapy with an expression plasmid for the interleukin-1 receptor antagonist. *Gene Therapy*, 10: 1543-1550

66. J-M. Kim, S-H. Ho, W. Hahn, J-G. Jeong, E-J. Park, H-J. Lee, S. S. Yu, C-S Lee, Y-W. Lee and **S. Kim** (2003) Electro-gene therapy of collagen-induced arthritis by using an expression plasmid for the soluble p75 tumor necrosis factor receptor-Fc fusion protein. *Gene Therapy*, 10: 1216-1224

65. M. Jin, H. Jeon, H. J. Jung, C-Y. Kang and **S. Kim** (2003) Enhancement of repopulation and hematopoiesis of bone marrow cells in irradiated mice by oral administration of PG101, a water-soluble extract from lentinus lepideus. *Experimental Biology and Medicine*, 228: 759-766

64. M. Jin, H. J. Jung, J. J. Choi, H. Jeon, J. H. Oh, K. Yoon and **S. Kim** (2003) Activation of selective transcription factors and cytokines by water-soluble extract from Lentinus lepideus. *Experimental Biology and Medicine*, 228: 749-758

63. S. S. Yu, E. Han, Y. Hong, J. Lee, and **S. Kim** (2003) Construction of a retroviral vector production system with the minimum possibility of a homologous recombination. *Gene Therapy*, 10: 706-711

62. S. Shin, M. Jin, H. J. Jung, B. Kim, H. Jeon, J. J. Choi, J. M. Kim, B. W. Cho, S. H. Chung, Y. W. Lee, Y. W. Song and **S. Kim** (2003) Suppressive effect of PG201, an ethanol extract from herbs, on collagen-induced arthritis in mice. *Rheumatology*, 42: 665-672

61. Y. Hong, S. S. Yu, J. Kim, K. Lee, C. B. Whitley, Y. Sugimoto, and **S. Kim** (2003) Construction of a high efficiency retroviral vector for gene therapy of Hunter's syndrome. *J. Gene Medicine*, 5: 18-29

60. J. O. Jeong, J. Byun, E-S Jeon, H-C Gwon, Y. S. Lim, J. Park, S-J Yeo, Y. J. Lee, **S. Kim** and D-K Kim (2002) Improved expression by cytomegalovirus promoter/enhancer and behavior of vascular endothelial growth factor gene after myocardial injection of naked DNA.

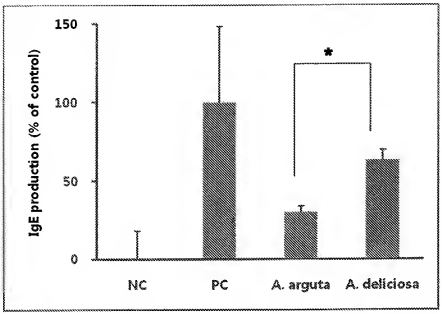
Experimental and Molecular Medicine, 34: 278-284
59. S. H. Kim, E. Lechman, **S. Kim**, J. Nash, T. Oligino, and P. D. Robbins (2002) Ex vivo gene delivery of IL-1 Ra and soluble sTNF Receptor confers a distal synergistic therapeutic effect in antigen-induced arthritis. *Molecular Therapy*, 6: 591-600
58. S. H. Kim, **S. Kim**, T. Oligino, and P. D. Robbins (2002) Effective treatment of established mouse collagen-induced arthritis by systemic administration of dendritic cells genetically modified to express FasL. *Molecular Therapy*, 6: 584-590
57. Lee, Y.T., Jeon, K.P., Lee, J.T., **S. Kim**, and Kim, V.N. (2002) MicroRNA maturation: stepwise processing and subcellular localization. *EMBO Journal*, 21:4663-4670
56. Lim, B. K., S. C. Choe, J. O. Shin, S. H. Ho, J. M. Kim, S. S. Yu, **S. Kim**, and E. S. Jeon. (2002) Local expression of interleukin-1 receptor antagonist by plasmid DNA improves mortality and decreases myocardial inflammation in experimental coxsackieviral myocarditis. *Circulation* 105:1278-81.
55. Kim, J. M., S. H. Ho, E. J. Park, W. Hahn, H. Cho, J. G. Jeong, Y. W. Lee, and S. **Kim**. (2002) Angiostatin gene transfer as an effective treatment strategy in murine collagen-induced arthritis. *Arthritis and Rheum*. 46:793-801.
54. Yoon, K., J. G. Jeong, and **S. Kim**. (2001) Stable expression of human immunodeficiency virus type 1 Nef confers resistance against Fas-mediated apoptosis. *AIDS Res Hum Retroviruses* 17:99-104.
53. Yoon, K., J. G. Jeong, H. Yoon, J. S. Lee, and **S. Kim**. (2001) Differential effects of primary human immunodeficiency virus type 1 nef sequences on downregulation of CD4 and MHC class I. *Biochem Biophys Res Commun* 284:638-42.
52. Park, S. W., H. C. Gwon, J. O. Jeong, J. Byun, H. S. Kang, J. R. You, S. S. Cho, M. J. Lee, Y. Lee, **S. Kim**, and D. K. Kim. (2001) Intracardiac echocardiographic guidance and monitoring during percutaneous endomyocardial gene injection in porcine heart. *Hum Gene Therapy* 12:893-903.
51. Kim, S. H., **S. Kim**, C. H. Evans, S. C. Ghivizzani, T. Oligino, and P. D. Robbins. (2001) Effective treatment of established murine collagen-induced arthritis by systemic administration of dendritic cells genetically modified to express IL-4. *J Immunol* 166:3499-505.
50. Kang, W. K., C. Park, H. L. Yoon, W. S. Kim, S. S. Yoon, M. H. Lee, K. Park, K. Kim, H. S. Jeong, J. A. Kim, S. J. Nam, J. H. Yang, Y. I. Son, C. H. Baek, J. Han, H. J. Ree, E. S. Lee, S. H. Kim, D. W. Kim, Y. C. Ahn, S. J. Huh, Y. H. Choe, J. H. Lee, M. H. Park, G. S. Kong, E. Y. Park, Y. K. Kang, Y. J. Bang, N. S. Paik, S. N. Lee, **S. Kim**, P. D. Robbins, H. Tahara, M. T. Lotze, and C. H. Park. (2001) Interleukin 12 gene therapy of cancer by peritumoral injection of transduced autologous fibroblasts: outcome of a phase I study. *Hum Gene Therapy* 12:671-84.
49. Gwon, H. C., J. O. Jeong, H. J. Kim, S. W. Park, S. H. Lee, S. J. Park, J. E. Huh, Y. Lee, **S. Kim**, and D. K. Kim. (2001) The feasibility and safety of fluoroscopy-guided percutaneous intramyocardial gene injection in porcine heart. *Int J Cardiol* 79:77-88.
48. Yu, S. S., J. M. Kim, and **S. Kim**. (2000) High efficiency retroviral vectors that contain no viral coding sequences. *Gene Therapy* 7:797-804.
47. Yu, S. S., J. M. Kim, and **S. Kim**. (2000) The 17 nucleotides downstream from the env gene stop codon are important for murine leukemia virus packaging. *J Virol* 74:8775-80.
46. Lee, Y., E. J. Park, S. S. Yu, D. K. Kim, and **S. Kim**. (2000) Improved expression of vascular endothelial growth factor by naked DNA in mouse skeletal muscles: implication for gene therapy of ischemic diseases. *Biochem Biophys Res Commun* 272:230-5.
45. Laufs, S., S. H. Kim, **S. Kim**, N. Blau, and B. Thony. (2000) Reconstitution of a metabolic pathway with triple-cistronic IRES- containing retroviral vectors for correction of tetrahydrobiopterin deficiency. *J Gene Med* 2:22-31.

44. Kim, S. H., C. H. Evans, **S. Kim**, T. Oligino, S. C. Ghivizzani, and P. D. Robbins. (2000) Gene therapy for established murine collagen-induced arthritis by local and systemic adenovirus-mediated delivery of interleukin-4. *Arthritis Res* 2:293-302.
43. Kim, S. H., **S. Kim**, and P. D. Robbins. (2000) Retroviral vectors. *Adv Virus Res* 55:545-63.
42. Kim, J. M., Y. Hong, K. Semba, and **S. Kim**. (2000) Physical and functional interaction between the HCMV IE2 protein and the Wilms' tumor suppressor WT1. *Biochem Biophys Res Commun* 267:59-63.
41. Kim, J. M., Y. Hong, K. T. Jeang, and **S. Kim**. (2000) Transactivation activity of the human cytomegalovirus IE2 protein occurs at steps subsequent to TATA box-binding protein recruitment. *J Gen Virol* 81:37-46.
40. Kim, J. M., Y. Hong, and **S. Kim**. (2000) Artificial recruitment of Sp1 or TBP can replace the role of IE1 in the synergistic transactivation by IE1 and IE2. *Biochem Biophys Res Commun* 269:302-8.
39. Gambotto, A., S. H. Kim, **S. Kim**, and P. D. Robbins. (2000) Methods for constructing and producing retroviral vectors. *Methods Mol Biol* 135:495-508.
38. Yoon, K., and **S. Kim**. (1999) Lack of negative influence on the cellular transcription factors NF- kappaB and AP-1 by the nef protein of human immunodeficiency virus type 1. *J Gen Virol* 80:2951-6.
37. Kim, J. M., Y. Hong, **S. Kim**, M. H. Cho, M. Yoshida, K. T. Jeang, and W. Burns. (1999) Sequences downstream of the RNA initiation site of the HTLV type 1 long terminal repeat are sufficient for trans-activation by human cytomegalovirus immediate-early proteins. *AIDS Res Hum Retroviruses* 15:545-50.
36. **S. Kim**, S. S. Yu, I. S. Lee, S. Ohno, J. Yim, and H. S. Kang. (1999) Human cytomegalovirus IE1 protein activates AP-1 through a cellular protein kinase(s).*J Gen Virol* 80:961-9.
35. Yoon, K., H. W. Kestler, and **S. Kim**. (1998) Growth properties of H5IVnef: HIV-1 containing the nef gene from pathogenic molecular clone SIVmac239. *Virus Res* 57:27-34.
34. Lee, H., **S. Kim**, M. Kang, W. Kim, and B. Cho. (1998) Prevalence of human foamy virus-related sequences in the Korean population. *J Biomed Sci* 5:267-73.
33. Kim, S. H., S. S. Yu, J. S. Park, P. D. Robbins, C. S. An, and **S. Kim**. (1998) Construction of retroviral vectors with improved safety, gene expression, and versatility. *J Virol* 72:994-1004.
32. Kang, M. R., Y. K. Cho, J. Chun, Y. B. Kim, I. Lee, H. J. Lee, S. H. Kim, Y. K. Kim, K. Yoon, J. M. Yang, J. M. Kim, Y. O. Shin, C. Kang, J. S. Lee, K. W. Choi, D. G. Kim, W. M. Fitch, and **S. Kim**. (1998) Phylogenetic analysis of the nef gene reveals a distinctive monophyletic clade in Korean HIV-1 cases. *J Acquir Immune Defic Syndr Hum Retrovirol* 17:58-68.
31. Byun, J., J. M. Kim, P. D. Robbins, and **S. Kim**. (1998) The selectable marker neo gene down-regulates gene expression from retroviral vectors containing an internal ribosome entry site. *Gene Ther* 5:1441-4.
30. Yoo, Y. D., C. J. Chiou, K. S. Choi, Y. Yi, S. Michelson, **S. Kim**, G. S. Hayward, and S. J. Kim. (1996) The IE2 regulatory protein of human cytomegalovirus induces expression of the human transforming growth factor beta1 gene through an Egr-1 binding site. *J Virol* 70:7062-70.
29. Lee, S. G., **S. Kim**, P. D. Robbins, and B. G. Kim. (1996) Optimization of environmental factors for the production and handling of recombinant retrovirus. *Appl Microbiol Biotechnol* 45:477-83.
28. Kim, S., S. S. Yu, and Y. N. Kim. (1996) Essential role of NF-kappa B in transactivation of the human immunodeficiency virus long terminal repeat by the human cytomegalovirus 1E1 protein. *J Gen Virol* 77:83-91.
27. Jin, M., **S. Kim**, and B. K. Kim. (1996) Induction of B cell proliferation and NF-kappa B

activation by a water soluble glycan from Lentinus lepideus. *Int J Immunopharmacol* 18:439-48.
26. Byun, J., J. M. Kim, S. H. Kim, J. Yim, P. D. Robbins, and **S. Kim.** (1996) A simple and rapid method for the determination of recombinant retrovirus titer by G418 selection. *Gene Ther* 3:1018-20.
25. Byun, J., S. H. Kim, J. M. Kim, S. S. Yu, P. D. Robbins, J. Yim, and **S. Kim.** (1996) Analysis of the relative level of gene expression from different retroviral vectors used for gene therapy. *Gene Ther* 3:780-8.
24. Choi, K. S., S. J. Kim, and **S. Kim.** (1995) The retinoblastoma gene product negatively regulates transcriptional activation mediated by the human cytomegalovirus IE2 protein. *Virology* 208:450-6.
23. Cannon, P., S. H. Kim, C. Ulich, and **S. Kim.** (1994) Analysis of Tat function in human immunodeficiency virus type 1- infected low-level-expression cell lines U1 and ACH-2. *J Virol* 68:1993-7.
22. Cannon, P. M., D. G. Tenen, M. B. Feinberg, H. S. Shin, and **S. Kim.** (1993) Human immunodeficiency virus-1 infection of the human promyelocytic cell line HL-60: high frequency of low-level infection and effect of subsequent cell differentiation. *Blood* 81:437-45.
21. Park, S. H., Y. M. Bae, T. J. Kim, I. S. Ha, **S. Kim,** J. G. Chi, and S. K. Lee. (1992) HLA-DR expression in human fetal thymocytes. *Hum Immunol* 33:294-8.
20. Luo, L., Y. Li, P. M. Cannon, **S. Kim,** and C. Y. Kang. (1992) Chimeric gag-V3 virus-like particles of human immunodeficiency virus induce virus-neutralizing antibodies. *Proc Natl Acad Sci U S A* 89:10527-31.
19. Lee, A. H., K. J. Lee, **S. Kim,** and Y. C. Sung. (1992) Transactivation of human immunodeficiency virus type 1 long terminal repeat-directed gene expression by the human foamy virus bel1 protein requires a specific DNA sequence. *J Virol* 66:3236-40.
18. Golden, M. P., **S. Kim,** S. M. Hammer, E. A. Ladd, P. A. Schaffer, N. DeLuca, and M. A. Albrecht. (1992) Activation of human immunodeficiency virus by herpes simplex virus. *J Infect Dis* 166:494-9.
17. Sakaguchi, M., B. Zenzie-Gregory, J. E. Groopman, S. T. Smale, and S. Kim. (1991) Alternative pathway for induction of human immunodeficiency virus gene expression: involvement of the general transcription machinery. *J Virol* 65:5448-56.
16. Mellor, J., C. Midgely, A. J. Kingsman, S. M. Kingsman, and S. Kim. (1991) Transcriptional activation by upstream activator sequences requires distinct interactions with downstream elements in the yeast TRP1 promoter. *Mol Gen Genet* 225:217-24.
15. Klotman, M. E., **S. Kim,** A. Buchbinder, A. DeRossi, D. Baltimore, and F. Wong-Staal. (1991) Kinetics of expression of multiply spliced RNA in early human immunodeficiency virus type 1 infection of lymphocytes and monocytes. *Proc Natl Acad Sci U S A* 88:5011-5.
14. Harbison, M. A., **S. Kim,** J. M. Gillis, and S. M. Hammer. (1991) Effect of the calcium channel blocker verapamil on human immunodeficiency virus type 1 replication in lymphoid cells. *J Infect Dis* 164:53-60.
13. Smith, J. S., S. Kim, and M. J. Roth. (1990) Analysis of long terminal repeat circle junctions of human immunodeficiency virus type 1. *J Virol* 64:6286-90.
12. **Kim. S.,** K. Ikeuchi, J. Groopman, and D. Baltimore. (1990) Factors affecting cellular tropism of human immunodeficiency virus. *J Virol* 64:5600-4.
11. Ikeuchi, K., **S. Kim,** R. A. Byrn, S. R. Goldring, and J. E. Groopman. (1990) Infection of nonlymphoid cells by human immunodeficiency virus type 1 or type 2. *J Virol* 64:4226-31.
10. Kim. S., R. Byrn, J. Groopman, and D. Baltimore. (1989) Timing of DNA and RNA synthesis during a one-step growth cycle of HIV. pp109-120. In: "UCLA Symposia on Molecular and Cellular Biology, New Series", Vol. 119, Alan R. Liss, Inc., New York.

09. Kim. S., K. Ikeuchi, R. Byrn, J. Groopman, and D. Baltimore. (1989) Lack of a negative influence on viral growth by the nef gene of human immunodeficiency virus type 1. *Proc Natl Acad Sci U S A* 86:9544-8.
08. Kim., S. Y., R. Byrn, J. Groopman, and D. Baltimore. (1989) Temporal aspects of DNA and RNA synthesis during human immunodeficiency virus infection: evidence for differential gene expression. *J Virol* 63:3708-13.
07. Neer, E. J., S. Y. Kim, S. L. Ang, D. B. Bloch, K. D. Bloch, Y. Kawahara, C. Tolman, R. Lee, D. Logothetis, D. Kim, and et al. (1988) Functions of G-protein subunits. *Cold Spring Harb Symp Quant Biol* 53:241-6.
06. Kim, S. Y., S. L. Ang, D. B. Bloch, K. D. Bloch, Y. Kawahara, C. Tolman, R. Lee, J. G. Seidman, and E. J. Neer. (1988) Identification of cDNA encoding an additional alpha subunit of a human GTP-binding protein: expression of three alpha i subtypes in human tissues and cell lines. *Proc Natl Acad Sci U S A* 85:4153-7.
05. Kim, S. Y., J. Mellor, A. J. Kingsman, and S. M. Kingsman. (1988) An AT rich region of dyad symmetry is a promoter element in the yeast TRP1 gene. *Mol Gen Genet* 211:472-6.
04. Harrison, S. M., K. L. Gearing, S. Kim, A. J. Kingsman, and S. M. Kingsman. (1987) Multiple cis-active elements in the long control region of bovine papillomavirus type 1 (BPV-1). *Nucleic Acids Res* 15:10267-84.
03. Osley, M. A., J. Gould, S. Kim, M. Y. Kane, and L. Hereford. (1986) Identification of sequences in a yeast histone promoter involved in periodic transcription. *Cell* 45:537-44.
02. Ogden, J. E., C. Stanway, S. Kim, J. Mellor, A. J. Kingsman, and S. M. Kingsman. (1986) Efficient expression of the Saccharomyces cerevisiae PGK gene depends on an upstream activation sequence but does not require TATA sequences. *Mol Cell Biol* 6:4335-43.
01. Kim, S., J. Mellor, A. J. Kingsman, and S. M. Kingsman. (1986) Multiple control elements in the TRP1 promoter of Saccharomyces cerevisiae. *Mol Cell Biol* 6:4251-8.

Exhibit B

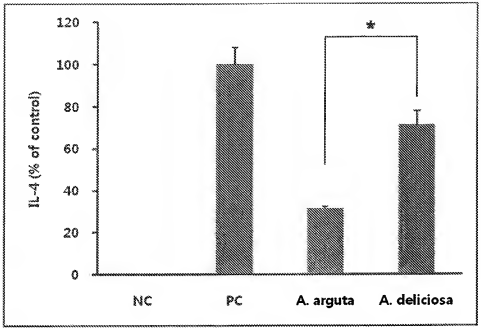


* $p<0.05$

NC = Negative Control

PC = Positive Control

Exhibit C



* $p<0.05$

NC = Negative Control

PC = Positive Control